510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
DEVICE ONLY TEMPLATE

A. 510(k) Number:
K033745

B. Purpose for Submission:
To obtain original clearance using traditional 510(k) for this new assay.

C. Analyte:
Troponin

D. Type of Test:
Immunochromatographic fluorescence immunoassay

E. Applicant:
RESPONSE BIOMEDICAL CORP.

F. Proprietary and Established Names:
RAMP TROPONIN I ASSAY

G. Regulatory Information:

1. Regulation section:
   21CFR §862.1215 -Creatine phosphokinase/creatine kinase or isoenzymes test system.
2. Classification:
   2
3. Product Code:
   MMI
4. Panel:
   CH

H. Intended Use:

1. Indication(s) for use:
   The RAMP Troponin I Assay is a quantitative immunochromatographic test indicated for use as an in vitro diagnostic product used with the RAMP Clinical Reader to measure cardiac troponin I levels in EDTA whole blood. Measurement of cardiac troponin I aids in the rapid diagnosis of acute myocardial infarction (AMI).
2. Special condition for use statement(s):
   The RAMP Troponin I Assay is intended to be used only to prioritize patient management for those suspected of AMI.
3. Special instrument Requirements:
   RAMP® Clinical Reader

I. Device Description:

The RAMP Troponin I Assay is a quantitative immunochromatographic test for the determination of TnI levels in EDTA whole blood. Diluted EDTA whole blood is added to the sample well of the Test Cartridge which houses the immunochromatographic test strip. The red blood cells are retained in the sample pad, and the separated plasma migrates along the strip. Fluorescent-dyed latex particles coated with anti-TnI antibodies bind to TnI, if present in the sample. As the sample migrates along the strip, TnI bound particles are immobilized at the detection zone, and additional particles are immobilized at the internal control zone.

The RAMP Clinical Reader then measures the amount of fluorescence emitted by the complexes bound at the detection zone and at the internal control zone. Using a ratio between the two fluorescence values, a quantitative reading is calculated.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Immunoassay: Triage Cardiac Panel®; Troponin I Assay (K973126) which is currently being marketed by Biosite Diagnostics, Inc.

   Immunoassay: Dimension® RxL Cardiac Troponin-I Flex®, (K973650) which is currently being marketed by Dade Behring Inc.

2. Predicate K number(s):
   K973126
   K973650
3. Comparison with predicate:

   The RAMP Troponin I Assay, Triage Cardiac Panel (Triage) Troponin I, and Dade Dimension RxL (Dimension) Cardiac Troponin-I (Troponin I) Flex Assays are for the quantitative measurement of TnI in human whole blood (RAMP and Triage) or plasma (Triage and Dimension). All three immunoassays utilize the binding of TnI to specific antibodies and utilize light in their respective detection systems. Both the RAMP and Triage assays measure light production from a fluorescence reaction using a fluorometer while the Dimension measures the amount of colored product produced which is directly proportional to the concentration of TnI present in the patient sample. Both the RAMP Troponin I and the Triage Troponin I assays are quantitative immunochromatographic tests, whereas the Dimension Troponin I test is a sandwich enzyme immunoassay.

   An additional minor difference is that while both the RAMP Troponin I and the Dimension Troponin I are single tests for TnI determination, the Triage Cardiac Panel consists of three tests, TnI, Creatine Kinase MB and Myoglobin.

Similarities		
Item	**Device**	**Predicate**
Intended Use	The RAMP Troponin I Assay is a quantitative immunochromatographic test indicated for use as an in vitro diagnostic product used with the RAMP Clinical Reader to measure cardiac troponin I (TnI) levels in EDTA whole blood. Measurement of TnI aids in the rapid diagnosis of acute myocardial infarction (AMI).	Triage Cardiac Panel is a fluorescence immunoassay used for the quantitative determination of TnI, Creatine Kinase MB and Myoglobin in heparinized whole blood and plasma specimens. The test is used as an aid in the diagnosis of myocardial infarction.
Test Principle	Immunochromatographic fluorescence immunoassay	Same
Target Population	Suspected Acute Myocardial Infarction	Same
Test Procedure	Add sample to Test Cartridge	Same
Automated Processing	Instrument transport of Test Cartridge within reader only moving step No internal liquid handling One step immunochromatography assay requiring no additional washes	Same
Read Results	Read results on screen	same
Test Time	19 minutes after Test Components come to room temperature	15 – 18 minutes after Test Device comes to room temperature
Waste Handling	Dispose of Test Cartridge as per correct institutional biohazard procedure	same
Automated Analysis	Yes	Yes
Self Contained	Yes	Yes
Portable	Yes	Yes
Battery Operation Available	Yes, rechargeable	Yes, replaceable
Special Instrumentation Required	Yes; RAMP Clinical Reader	Yes; Triage Meter

Differences		
Item	**Device**	**Predicate**
Sample Preparation	Use provided pipette to dilute sample 1/3 in provided pre-measured diluent vial	Use special provided transfer pipette to withdraw sample to the level of the lower bulb
Specimen Type	Whole anticoagulated blood (EDTA)	Whole anticoagulated blood or plasma (heparin)
Specimen Storage: Ambient 2-8 ºC -20 ºC	 up to 2 hours up to 2 days not recommended	 not recommenced up to 24 hours for longer term storage (plasma only)

K. Standard/Guidance Document Referenced (if applicable):
None Referenced

L. Test Principle:
Immunochromatographic fluorescence immunoassay

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

The intra-assay and the inter-assay precision of the RAMP Troponin I Assay were determined using the NCCLS EP-5 protocol by one operator assaying duplicates of control materials and human plasma pools twice each day over 10 days (concentrations of 5.01, 1.05, 0.70, 0.40, 0.29 and 0.22 ng/mL TnI). The mean, standard deviation and % CV were calculated for the predicted TnI at each concentration.

Precision	**Standards TnI Mean Concentration (ng/mL)**					
	5.01	**1.05**	**0.70**	**0.40**	**0.29**	**0.22**
Within Run Precision	8.3%	8.7%	6.5%	5.3%	9.3%	7.2%
Total Precision	8.3%	10.0%	8.4%	7.4%	10.0%	11.4%

b. Linearity/assay reportable range:

TnI antigen concentrations of 0.86, 1.72, 3.44, 6.88, 13.75, and 25.50 ng/mL were prepared in normal donor EDTA blood. The linearity and percent recovery were determined by assaying five replicates of each concentration and baseline. The mean, standard deviation and %CV were calculated for the predicted TnI at each concentration. Linear regression analysis of actual TnI concentration versus

expected TnI concentration resulted with an R = 0.997 and a slope of 1.019 with an offset of 0.279. The recovery of spiked TnI antigen at the five concentrations ranged from 95 to 115% with an average of 105%.

c. *Traceability (controls, calibrators, or method):*
Each RAMP Troponin I kit includes a Lot Card that is individually packaged in an anti-static pouch. The Lot Card provides information specific to the kit Test Cartridge lot, including lot number, expiration date, and standard curve information. Insertion of the Lot Card into the Reader is the only calibration necessary for each lot of reagents.

Quality Controls are provided in every Test Cartridge, which serve as built-in performance controls for routine QC requirements. A comparison of this control and the assay result indicate that sufficient sample was applied to the test device, that unbound fluorescent label washed sufficiently from the detection zone, and the device was inserted and read properly by the instrument. This control also prevents a used cartridge from being re-run by the reader. Antibody quality, system function and assay timing are checked on each assay run. An unacceptable result from the control displays a warning message on the instrument indicating that the test should be repeated.

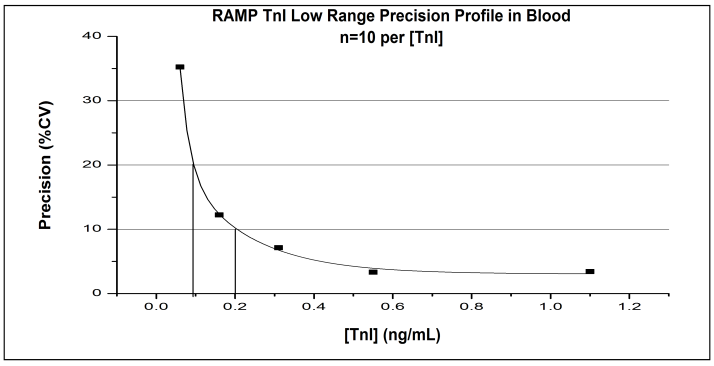
It is recommended that a commercial external control material be run in the RAMP Troponin I Assay weekly, or in conformance with regulatory or accreditation requirements. To run a QC sample, follow the instructions under the SAMPLE ANALYSIS PROCEDURE section. Treat the control as a whole blood sample.

d. *Detection limit:*
The lower limit of detection (LLD) is defined as the analyte concentration corresponding to the mean (n=20) plus 2 standard deviations of the zero. The LLD of the RAMP Troponin I Assay is 0.03 ng/mL TnI, the lowest TnI level that can be distinguished from zero.

Another characteristic of an analytical measurement is the functional sensitivity, which is defined as the TnI level at which the test method displays a particular percent coefficient of variation (%CV). Estimates of the 20% and 10% functional sensitivities for the RAMP Troponin I Assay were determined from whole blood estimates. The 20% and 10% functional sensitivities are 0.1 ng/ml and 0.21 ng/mL TnI, respectively (see graph below).

TnI values below the 20% functional sensitivity should be reported as less than (<) 0.10 ng/mL, instead of the numerical value. TnI

levels in excess of 32 ng/mL are reported as greater than (>) 32 ng/mL.



e. Analytical specificity:

Potentially cross-reactive substances were evaluated by spiking different concentrations into blood. Skeletal Troponin I, Cardiac Troponin T and Cardiac Troponin C appear to have no significant cross-reactivity with the RAMP Troponin I Assay. HAMA, HAGA, HARA and RhF appear to have minimal cross-reactivity with the RAMP Troponin I Assay.

Potentially interfering substances were evaluated by spiking different concentrations of potential interferents into EDTA blood with TnI added. Different blood samples were used for each potential interferent.

Interference was evaluated by calculating the TnI concentration of potential interferent-spiked blood, expressed as a percentage of the TnI concentration of the unspiked (no potential interferent) blood sample. No evidence of cross-reactivity or interference was observed for hemoglobin, triglyceride, bilirubin, cholesterol, or heparin at levels of very high physiological concentrations, up to 1500 mg/dL, 3000mg/dL, 80 mg/dL, 500 mg/dL, and 66 IU/mL, respectively. No trend was observed in the TnI predictions as the concentration of potential interferent was increased.

f. Assay cut-off:

0.10 ng/mL

2. <u>Comparison studies:</u>

a. Method comparison with predicate device:

Three hundred and sixty-five (365) subjects were enrolled in the Method Comparison Study. Of these subjects, 180 were normal individuals (84 males and 96 females) and 185 were suspected of acute myocardial infarct (AMI) based on the individual hospital criteria (115 males and 70 females). EDTA and heparin whole blood samples were obtained for each of these subjects. All normal subjects were consented. Waste samples were used for the subjects suspected of AMI. An aliquot of the whole blood was taken for the

RAMP Troponin I Assay and heparinized plasma was prepared for the Dade Behring Dimension Cardiac Troponin-I Flex Assay. To accommodate the differing reportable ranges of the RAMP Troponin I and the Dimension Cardiac Troponin-I Flex Assay, the data was winsorized, and then examined for outliers. One outlier was removed from the suspect AMI population. The correlation data is presented in the table below.

Population	n	Sy.x	Slope y =	Intercept	R
Combined Populations	364	0.94	0.456	0.011	0.988
Suspect AMI Subjects	184	1.33	0.456	0.025	0.986

The sensitivity, specificity, and percent agreement of all samples were calculated comparing a clinical cutoff of 0.3 ng/mL TnI for the RAMP Troponin I Assay to the published clinical cutoff of 0.6 ng/mL TnI presented in the Dade Dimension package insert. The data is presented in the table below.

	n	(%)	s.e.	95 % CI	
Sensitivity	136	94.85	1.90	91.14	98.57
Specificity	229	98.25	0.87	96.56	99.95
PV+	133	96.99	1.48	94.09	99.90
PV-	232	96.98	1.12	94.78	99.18
Concordance	365	96.99	0.90	95.23	98.74

b. Matrix comparison:
Not Applicable

3. Clinical studies:
   a. Clinical sensitivity:
   Not Applicable
   b. Clinical specificity:
   Not Applicable
   c. Other clinical supportive data (when a and b are not applicable):
   Not Applicable
4. Clinical cut-off:
   Not Applicable
5. Expected values/Reference range:
   One hundred and eighty (180) normal individuals were enrolled in the Expected Values Study. The 99% reference range of results were < 0.1 ng/mL for the RAMP Troponin I Assay.

N. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.